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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Paper No. 050504

Application Number: 09/609,543
Filing Date: July 03, 2000
Appellant(s): JEFFERS ET AL.

Ivor R. Elrifi and Naomi Biswas
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed 24 February 2004.

(1) Real Party in Interest

A statement identifying the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

A statement identifying the related appeals and interferences which will directly affect or be directly affected by or have a bearing on the decision in the pending appeal is contained in the brief.

(3) Status of Claims

The statement of the status of the claims contained in the brief is correct.

(4) Status of Amendments After Final

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

(5) Summary of Invention

The summary of invention contained in the brief is deficient because of the statement "Applicants .... disclose that the FGF-CX polypeptide has utility in promoting growth of cells in the vicinity of a wound, cells in the vascular system, cells involved in hematopoiesis, cells involved in erythropoiesis, cells in the lining of the gastrointestinal tract, and cells in hair follicles". Whether the claimed invention has utility in promoting growth of cells as asserted in the instant specification is the issue before the Board

(6) Issues

The appellant's statement of the issues in the brief is correct.

(7) Grouping of Claims

Appellant's brief includes a statement that the claims do stand or fall together and provides reasons as set forth in 37 CFR 1.192(c)(7) and (c)(8).

(8) Claims Appealed

The copy of the appealed claims contained in the Appendix to the brief is correct.

(9) Prior Art of Record

JEFFERS et al. Gastroenterology 123: 1151-1162, 2002.

GALZIE et al. Biochem. Cell. Biol. 75: 669-685, 1997.

(10) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claims 1, 5, 41, 46 and 63-64 are rejected under 35 U.S.C. §101 because the claimed invention is drawn to an invention with no apparent or disclosed specific and substantial credible utility.

It is clear from the instant specification that the "FGF-CX" protein (SEQ ID NO:2) described therein is what is termed an "orphan protein" in the art. This is a protein whose cDNA has been isolated because of its similarity to known proteins. There is

little doubt that, after complete characterization, this protein, and the nucleic acid encoding it, may be found to have a specific and substantial credible utility. This further characterization, however, is part of the act of invention and until it has been undertaken, the claimed invention is incomplete. The instant situation is directly analogous to that which was addressed in *Brenner v. Manson*, 148 U.S.P.Q. 689 (Sus. Ct, 1966), in which a novel compound which was structurally analogous to other compounds which were known to possess anti-cancer activity was alleged to be potentially useful as an anti-tumor agent in the absence of evidence supporting this utility. The court expressed the opinion that all chemical compounds are "useful" to the chemical arts when this term is given its broadest interpretation. However, the court held that this broad interpretation was not the intended definition of "useful" as it appears in 35 U.S.C. §101, which requires that an invention must have either an immediately obvious or fully disclosed "real world" utility. The court held that:

> "The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility", "[u]nless and until a process is refined and developed to this point-where specific benefit exists in currently available form-there is insufficient justification for permitting an applicant to engross what may prove to be a broad field", and "a patent is not a hunting license", "[i]t is not a reward for the search, but compensation for its successful conclusion."

The instant claims are drawn to a protein of as yet undetermined function or biological significance. There is absolutely no evidence of record or any line of reasoning that would support a conclusion that the "FGF-CX" protein of the instant application could be used in a method of diagnosing, treating, preventing, or delaying a tissue proliferation-associated disorder, such as "tumors, restenosis, psoriasis, Dupuytren's contracture, diabetic complications, Kaposi sarcoma, and rheumatoid arthritis" (see page 6, lines 3-7 of the specification), in a method of "treating a pathological state in a mammal" by administering the polypeptide (see page 5, line 6), in a method of "promoting growth of cells in a subject" wherein the cells are "in the vicinity of a wound, cells in the vascular system, cells involved in hematopoiesis, cells involved in erythropoiesis, cells in the lining of the gastrointestinal tract, and cells in hair follicles" (see page 5, lines 15-21), in "methods of diagnosing the presence or amounts of these compositions, in screening for and identifying therapeutic agents related to FGF-CX-associated pathologies, and in methods of treatment of various kinds of malignancy" (see sentence spanning pages 17-18), for use in screening assays, detection assays, predictive medicine, and methods of treatment (see sentence spanning pages 67-68), for stimulation of fibroblasts for use in wound healing (see page 76, lines 29-30), for stimulation of hematopoietic cells, immune system cells, and vascular smooth muscle cells, as well as for treating bone fractures and osteoporosis (see page 77, lines 1-3), diagnosis of cerebral tumors (page 77, lines 3-4), and for treatment of cancer (page 77, lines 9-13). Neither the specification nor the prior art demonstrates a causal correlation or nexus of the claimed polypeptide with any of the conditions or disorders contemplated by the

instant specification, therefore, there is no evidence of record that would provide for a method of treating/diagnosing any of the listed conditions or disorders. There is absolutely no evidence of record or any line of reasoning that would support a conclusion that the "FGF-CX" protein of the instant application is involved in regulating growth and/or differentiation of any *particular* cell population. The record fails to indicate any evidence of any of these biological activities, and it would appear that until some actual and specific significance can be attributed to the protein identified in the specification as FGF-CX, the gene encoding it, or the antibody that binds it, the instant invention is incomplete. The instant specification refers to "FGF-CX - like activities and physiological functions", but fails to describe what these activities or functions are. The specification asserts that the claimed protein will have activities similar to other FGF proteins based on amino acid sequence similarity, but it is not clear or predictive which activity of the FGF family will be possessed by the claimed protein based on structural similarity alone. The protein of the instant specification is a compound which is known to share some structural similarity to the FGF family of proteins which are known in the art to have biological significance in regulation of cell proliferation, differentiation, and function based on sequence similarity to members of the FGF-family. However, as indicated in Galzie et al. (Biochem. Cell Biol. 75: 669-685, 1997), the FGF family is complex and diverse (see abstract). Table 1 of Galzie et al. details the biological significance of the first 9 members of this protein family, wherein none of the associated functions are found in common with any other family member. In the absence of the knowledge of the biological significance of "FGF-CX", there is no immediately obvious

patentable use for it. The disclosed protein only shares approximately 70% amino acid sequence similarity/identity with the most closely related protein of the prior art. Based on this degree of sequence similarity, it is unlikely and unpredictable if any one biological activity of the prior art proteins will be possessed by the claimed invention. Furthermore, the prior art of record demonstrates that the biological function of the protein family to which the disclosed protein is said to be a member is so diverse, that one could not predict which biological activity is possessed by the disclosed protein based on structural similarity alone, especially since all the members share structural similarity, but not functional similarity. To employ the instant invention in any of the disclosed methods would clearly be using it as the object of further research which has been determined by the courts to be a utility which, alone, does not support patentability. Since the instant specification does not disclose a credible "real world" use for the claimed invention, it is incomplete and, therefore, does not meet the requirements of 35 U.S.C. §101 as being useful.

The instant specification provides data on expression of the claimed protein, indicating that it is expressed in normal cerebellum, as well as in several human tumor cell lines without being expressed in corresponding normal tissues. The specification provides a chromosomal location for the FGF-CX and "[e]xpression of heterologous FGF-CX in NIH 3T3 cells is found to induce their transformation and tumorigenicity" (see page 17, lines 15-16). However, these disclosed properties of the claimed protein, expression pattern and ability to transform fibroblast cells in culture does not provide a specific, substantial and credible utility for the claimed polypeptides. Expression of the

claimed polypeptide in cancer tissue does not establish a nexus between the claimed protein and cancer growth. Expression of the claimed polypeptide could just as likely be a result of the cancer, and not a causative agent, therefore one of ordinary skill in the art could not target the claimed polypeptide for treatment of the cancer. The instant specification fails to teach that the claimed polypeptide is diagnostic for any specific cancer, as it is found in normal and diseased tissue. The instant specification teaches that administration of the polypeptide stimulates proliferation of fibroblasts in culture, but these cells also lose contact inhibition, meaning that the cells take on a transformed phenotype. Therefore, the claimed polypeptide would not be considered useful for wound healing as asserted in the specification. Page 101 of the instant specification states "[s]pecific disease indications where therapeutic targeting of FGF-CX might be applied include adenocarcinomas of the colon, prostate, lung, kidney, uterus, breast, bladder, ovary" (see lines 26-28). However, in the absence of a nexus or correlation with a particular disease or cancer, the instant specification does not disclose a substantial "real world" use for the claimed invention, it is incomplete and, therefore, does not meet the requirements of 35 U.S.C. §101 as being useful.

Claims 1, 5, 41, 46, 63-64 are rejected under 35 U.S.C. §112, first paragraph, as failing to adequately teach how to use the instant invention for those reasons given above with regard to the rejection of these claims under 35 U.S.C. §101.

(11) Response to Argument

Issue #1 – Utility rejection

Appellant asserts at page 6 of the Brief that the specification makes a specific assertion of utility for the claimed invention in that the claimed protein "may be used to stimulate cell growth, including especially growth of fibroblasts and epithelial cells in the linings of the gastrointestinal tract". Appellant asserts that stimulation of cell growth is described in the specification at pages 102-104, especially example 10. Appellant concludes that this teaching is sufficient to provide an assertion of utility for the present invention, that the assertion identifies a specific utility which would be considered by those skilled in the art to be a substantial utility, and that the assertion is also a credible one. These arguments are not persuasive for the reasons detailed in the previous Office actions. The examples upon which Appellant's conclusions are based are not predictive of the biological activity of the claimed invention *in vivo.* Although the specification teaches that the claimed protein will stimulate proliferation of 3T3 cells *in vitro*, these cells also lose contact inhibition, meaning that the cells take on a transformed phenotype. The NIH 3T3 cells are a designated cell line which originated from fibroblast cells, however, they are cells which are no longer in their native environment and do not necessarily behave as a natural fibroblast cell would. The fact that the claimed protein of the instant invention transforms these cells as well as stimulates proliferation of these cells does not support the asserted uses of the claimed protein as disclosed in the instant specification. One of ordinary skill in the art at the time the invention was made would not conclude that the claimed protein could be used

for treating wounds of any particular tissue because the claimed protein appears to transform fibroblasts. This latter activity is not separable from the ability to stimulate proliferation, and the instant specification does not teach a utility for a protein which transforms cells as well as inducing proliferation. FGF proteins have a variety of activities based on the location of expression and the receptors to which the protein binds, therefore, without further information and evidence, one of ordinary skill in the art would not know what tissue would be affected by the claimed invention and the asserted utilities are not substantial at the time of the instant invention.

Appellant asserts that the claimed protein "has a credible utility in promoting growth of cells in the lining of the gastrointestinal tract in order to treat intestinal inflammation and ulcers" (see page 7 of the Brief). Appellant has also provided a post-filing date reference which demonstrates this activity for the claimed invention. Appellant then cites *In re Gottlieb* 328 F.2d 1016 (CCPA) and concludes that one specific utility is sufficient to meet the utility requirement (see page 8 of the Brief).

However, the facts of *Gottlieb* are different from the facts of the instant application. In *Gottlieb*, the specification contained evidence that the compound being claimed had anti-fungal activity as well as all three disclosed utilities being related to this biological activity. In the instant application, the specification contains no evidence of a particular biological activity and the asserted uses do not refer to a common biological activity; i.e. each specific asserted utility would need to be tested to confirm which asserted utility the claimed invention could be used for.

The instant specification asserts that the "FGF-CX" protein of the instant application could be used in a method of diagnosing a tissue proliferation-associated disorder, "such as tumors, restenosis, psoriasis, diabetic and post-surgery complications, and rheumatoid arthritis" (see page 4, lines 26-28 of the specification), in a method of "treating or preventing or delaying a tissue proliferation-associated disorder" (page 5, lines 28-29 of the specification) by administration of a FGF-CX nucleic acid, polypeptide or antibody, wherein the disorder includes tumors, restenosis, psoriasis, Dupuytren's contracture, diabetic complications, Kaposi sarcoma, and rheumatoid arthritis (see page 6, lines 6-7 of the specification), in a method of treating or diagnosing glia-associated disorders, including "cerebral lesions, cerebral edema, senile dementia, Alzheimer's disease, diabetic neuropathies, etc." (see page 58, lines 2-4), stimulating fibroblasts, megakaryocytes, hematopoietic cells, immune system cells, vascular smooth muscle cells treating bone fractures and osteoporosis, diagnosis and treatment of cerebral tumors (see page 58, lines 11-16). The fact that the specification also includes a recitation that the claimed invention may also stimulate cells of the gastrointestinal tract in addition to all of the other possible uses of the claimed invention does not appear to provide a substantial utility for the claimed invention as filed. A substantial utility is a utility that defines a "real world use". Utilities that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use are not substantial utilities. In the instant situation, the specification lists numerous uses for the claimed invention which are not linked by tissue type or mechanism of action; i.e. if the invention works for one of the asserted uses, then the

skilled artisan would have a reasonable expectation that it would work for the other asserted uses. Therefore, the skilled artisan would need to carry out further research on the claimed invention to determine which of the possible asserted uses the claimed invention could be used for; this does not constitute a disclosure of a substantial utility. Appellant's submitted Press Release has been noted, but again, it does not make up for the deficiencies of the original disclosure, which lacks a substantial utility at the time the instant invention was filed.

Appellant argues at page 9 of the Brief that "utility is also supported by the structural similarity of FGF-CX with other known members of the FGF family". This argument is not persuasive and has been addressed in previous Office actions. As illustrated by Galzie et al., the FGF family does not share the same specific, substantial and credible utility since they have distinct biological activities which cannot be predicted from their amino acid structure. The conservation of particular domains is not surprising for proteins in a family, wherein the family is defined by structural elements. However, the conservation of structure does not necessarily equate to conservation of function, as demonstrated by the prior art (see Galzie et al., Table 1). Appellant asserts that the claimed protein has a biological activity similar to a structurally related protein (FGF-9), however, these two proteins do not have the same utility since FGF-9 stimulates glial cells and the claimed protein does not. The ability of an FGF protein to stimulate endothelial cells is not a specific utility because the FGF proteins are specific for particular endothelial cells. For example, KGF stimulates keratinocytes but not fibroblasts, therefore, it cannot be used in the same way as an FGF which stimulates

fibroblasts. bFGF stimulates fibroblasts and FGF-9 stimulates glial cells, and therefore, they cannot be used for the same purpose. The members of the FGF family have divergent activities in that they typically stimulate particular cell types or act on particular tissues and they are not predictive of one another. The activities of some FGF proteins are pleiotropic whereas others only affect one specific tissue or function. Assignment to the FGF family is not predictive of a utility of stimulating cells of the GI tract because this is but one tissue of endothelial cell origin for which the FGF proteins are known to stimulate and the skilled artisan would need to carry out further research on the claimed invention to identify or reasonably confirm for which tissue the claimed invention would have a biological activity.

Appellant cites *In re Jolles* and *In re Brana* in support of a finding of utility in the instant application. In *In re Jolles*, 628 F.2d 1322, 206 USPQ 885 (CCPA 1980), pharmaceutical compositions were claimed that were disclosed to be useful in treating acute myeloblastic leukemia. *See id.* at 1323, 206 USPQ at 886. The active ingredients in the compositions were closely related to daunorubicin and doxorubicin, both of which were "well recognized in the art as valuable for use in cancer chemotherapy." *Id.,* 206 USPQ at 887. the applicant also submitted declaratory evidence showing that eight of the claimed compositions were effective in treating tumors in a mouse model, and one was effective in treating humans. *See id.* at 1323-24, 206 USPQ at 887-88. The Court noted that the data derived from the mouse model were "relevant to the treatment of humans and [were] not to be disregarded," id. at 1327, 206 UPSQ at 890, and held that the evidence was sufficient to support the

asserted therapeutic utility. *See id.* at 1327-28, 206 USPQ at 891. The instant case is distinguished from that of *Jolles* in that the structural similarity of the claimed compound to other FGF proteins does not provide for a specific, substantial and credible utility for the reasons of record (i.e. because the members of the FGF family do not share a common biological activity which equates to a specific, substantial and credible utility in common for the family). Appellant also refers to *In re Brana* 51 F.3d 1560, 34 USPQ2d 1436 (Fed. Cir. 1995), and states "evidence of success in structurally similar compounds is relevant in determining whether one skilled in the art would believe an asserted utility". This is not really the issue in the *Brana* case, but rather that human testing is not necessary to establish utility for a method of treatment. The invention claimed in *Brana* was a group of compounds disclosed to have antitumor activity. *See id.* at 1562, 34 USPQ2d at 1437-38. The specification disclosed that the claimed compounds had higher antitumor activity than related compounds known to have antitumor activity, and the applicants provided declaratory evidence of in vivo activity against tumors in a mouse model. *See id.*, 34 USPQ2d at 1438. The Court held that these data were sufficient to satisfy § 101; usefulness in patent law does not require that the invention be ready to be administered to humans. *See id.* at 1567, 34 USPQ2d at 1442. The instant application is distinguished from that of *Brana* in the fact that the instant specification contains no evidence of a particular biological activity to support any of the asserted, divergent utilities.

Therefore, the instant application as originally filed does not support a specific, substantial and credible utility for the claimed invention because the asserted utilities

require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use, and therefore are not substantial utilities.

Issue 2- 112/1st Paragraph rejection.

Appellant argues that a how to use rejection cannot stand because the instant situation does not meet the criterion of being totally incapable of achieving a useful result. This argument is not persuasive. Since the instant specification fails to provide a specific, substantial and credible utility for the claimed invention, the specification clearly does not teach how to use the claimed invention.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

Christine J. Saoud

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May 7, 2004

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